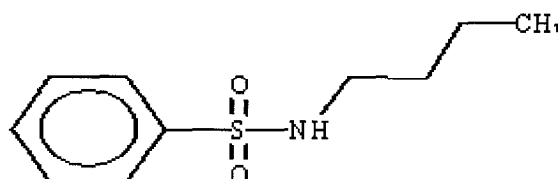


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N-n-Butylbenzenesulphonamide



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CAS Number 3622-84-2

U.S. EPA HPV Challenge program

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Executive Overview

N-n-Butylbenzenesulphonamide (BBSA) is a cyclic amide, produced out of the reaction of mono-N-Butylamine (CAS 109-73-9) with Benzenesulphonylchloride (CAS 98-09-9). The synthesis step is followed by a purification, drying and filtration step. BBSA is a clear colourless oily liquid which is almost odourless. It is primarily used as a plasticizer. The product has a low volatility and is practically insoluble in water.

Based on physico-chemical data, the product will not bio-accumulate in the environment ($\log P_{ow} = 2.1$). According to the fugacity model, it will be primarily distributed to the soil and water phase. BBSA will not hydrolyse under normal conditions, and it also proved to be not readily biodegradable.

The toxicity of BBSA to aquatic species is relatively low. The 48h EC₅₀ for Daphnia is 56 mg/l, the 72h EC₅₀ for algae is 83 mg/l.

The oral LD₅₀ of BBSA is 2070 mg/kg bw and the dermal LD₅₀ is greater than 2000 mg/kg bw which indicate a low acute toxicity. The acute inhalation toxicity (LC₅₀) is greater than 4.066 mg/l after 4 hours of exposure.

In a repeated dose study (28 days), the NOAEL was established at 50 mg/kg/day.

An *in vitro* genetic toxicity study showed that there is no mutagenic potential in the presence or absence of metabolic activation.

There were no studies available on *in vivo* genetic toxicology or on reproductive or developmental toxicity.

It is concluded that additional studies are needed for *in vivo* genetic toxicology and for reproductive or developmental toxicity. Two studies are recommended, OECD 473 (Chromosome aberration Test) and OECD 421 (Combined Reproduction / Developmental Screening Test), to fill the data elements of the HPV.

Data analysis

CAS Number 3622-84-2	Available	Estimation Method	Acceptable	Testing Recommended
N-Butylbenzenesulphonamide				
HPV endpoint				
Physical Chemical data				
Melting Point	Y		Y	N
Boiling Point	Y		Y	N
Vapor Pressure	Y		Y	N
Partition coefficient (octanol/water)	Y		Y	N
Environmental Fate				
Photo-Degradation		Y	Y	N
Abiotic Degradation-Hydrolysis	Y		Y	N
Biodegradation	Y		Y	N
Transport		Y	Y	N
Ecotoxicity				
Acute toxicity to Fish		Y	Y	N
Acute toxicity to Daphnia	Y	Y	Y	N
Acute toxicity to Algae	Y	Y	Y	N
Toxicity				
Acute toxicity	Y		Y	N
Repeated dose	Y		Y	N
Genetic toxicology in vitro	Y		Y	N
Genetic toxicology in vivo				Y
Reproductive Toxicity				Y
Developmental Toxicity				Y

Introduction

N-n-Butylbenzenesulphonamide (BBSA) is a clear, colourless, almost odourless oily liquid.

BBSA is used as a plasticizer in polyacetals, polycarbonates, polysulphones and in Nylon 11 and Nylon 12. As a plasticizer, it contributes the following properties on the above materials:

- easier removal from the mould
- easier machining
- a better finish due to more regular pore-size distribution
- good heat stability up to 180°C, and, in particular, a barrier to the absorption of water, whence an outstanding shape stability

Polyamide 11 and 12 compounds, containing BBSA, are used for flexible tubing used for example in flexodrilling. The extruded materials are distinguished by higher impact strength at low temperatures.

Another specific application of flexible polyamide tubing is the manufacture of compressed-air brake hoses for most heavy commercial vehicles.

Exposure is limited by process conditions, and controlled by using efficient exhaust when used at high temperature. No occupational exposure level set by a governmental organisation could be found for BBSA.

Common synonyms are N-n-Butylbenzenesulfonamide and N-n-Butylamide of benzenesulphonic acid.

Physicochemical data

Physicochemical data are available from tests done by the manufacturer or contract laboratories.

Table 1: Physicochemical properties	
Melting Point	-30°C
Boiling Point	> 250°C (1013 hPa)
Vapour Pressure	<0.001 hPa (20°C)
Octanol-Water Partition coefficient	Log Ko/w = 2.1 (8)
Water solubility	1.02 g/l (20°C)

These properties indicate that N-Butylbenzenesulphonamide is an involatile liquid, practically insoluble in water. The log Ko/w is smaller than 3, this indicates that there is a low potential for bioaccumulation.

Recommendation

The physico-chemical properties are well defined. No additional testing is needed for physico-chemical properties.

Environmental Fate

Photodegradation

The photodegradation rate was calculated using AOPWIN v1.90 (Atmospheric Oxidation Program for Microsoft Windows) (3) that estimates the rate constant for the atmospheric, gas-phase reaction between organic chemicals and photochemically produced hydroxyl radicals. The estimated rate constant is then used to calculate atmospheric half-life values for organic compounds based upon average atmospheric concentrations of hydroxyl radicals. AOPWIN calculated a rate constant of $13.83 \text{ E-12 cm}^3/\text{molecule}\cdot\text{sec}$.

Modeling the $T_{1/2}$ for the reaction of N-Butylbenzenesulphonamide with atmospheric hydroxyl radical at the EPA-accepted default concentration of 1,500,000 radicals per cubic centimeter results in an estimate of relatively short half-lives in air (9.28 hours)

Stability in water – Hydrolysis

Sulfonamides (like N-Butylbenzenesulphonamide) do not hydrolyse under normal condition (neutral aqueous environment) (1)

Transport between Environmental Compartments

The fugacity of N-Butylbenzenesulphonamide in the environment was estimated using the Mackay's EQC Level III Fugacity Model with the default values available in EPIWIN v3.10 (3). The measured $\log K_{ow}$ (2.1) was used for the calculation. The results for distribution using equal initial distribution to air, water soil and sediment are (in percent mass amount):

- Air 2.39%
- Water 42.3%
- Soil 55.2%
- Sediment 0.14%

EQC modeling predicts that the majority of the substance will be in the soil and water phase.

Biodegradation

Determination of the ready biodegradability has been done by the Carbon Dioxide (CO₂) Evolution Test (Modified Sturm Test).⁽⁹⁾ The average degradation values during the test period revealed 18% degradation.

N-Butylbenzenesulphonamide was not readily biodegradable under the conditions of the modified Sturm test.

In the toxicity control the substance was found not to be inhibitory.

Recommendation

No further tests on environmental fate are recommended.

Ecotoxicity

Acute Fish toxicity

No experimental data are available. The ECOSAR program predicts an acute toxicity value of 80.8 mg/l (LC₅₀, 96h).

Acute Daphnia toxicity

An acute toxicity study in *Daphnia magna* (static) with N-Butylbenzenesulphonamide is available. ⁽⁶⁾ Under the conditions of the study, the product did not induce acute immobilisation of *Daphnia magna* at 32 mg/l after 48 hours of exposure (NOEC). The 48h-EC₅₀ was 56 mg/l based on nominal concentrations (95% confidence interval between 49 and 69 mg/l).

Freshwater Algae inhibition

A Fresh water algae growth inhibition test is available for N-Butylbenzenesulphonamide. ⁽¹⁰⁾ Under the conditions of the study with *Selenastrum capricornutum*, the NOEC for cell growth inhibition was determined to be 22 mg/l and the NOEC for growth rate reduction was 10 mg/l. The EC₅₀ for cell growth inhibition (EbC₅₀:0-72h) was 49 mg/l. The EC₅₀ for growth rate reduction (ErC₅₀:0-72h) was 83 mg/l.

The U.S. EPA has developed a SAR relationship for aquatic toxicity that shows a good correlation for this compound in relation with experimental data for *Daphnia* and Algae toxicity.

In Table, the values from experimental data and ECOSAR predictions are listed.

Table 2: SAR and experimental toxicity values

	Experimental values	ECOSAR Prediction (3)
Fish, LC50 (96h)	-	80.8 mg/l
Daphnia, EC50 (48h)	56 mg/l	88.5 mg/l
Algae, EC50 (72h)	49 mg/l	56.3 mg/l

Recommendation

From the table it can be concluded that the predictions from ECOSAR are very close to the experimental values. N-Butylbenzenesulphonamide is most toxic to freshwater algae. According to ECOSAR, the toxicity to Fish lies between the toxicity to Algae and the toxicity to Daphnia. The data available from SAR and experimental toxicity values fill the HPV required endpoints. It is recommended that no additional studies be conducted.

Health effects

Acute toxicity

Study reports on acute toxicity are available for N-Butylbenzenesulphonamide. The acute oral toxicity study on rats reported an LD50 of 2070 mg/kg bw. (5) Acute dermal toxicity is measured in rats and indicates an LD50 greater than 2000 mg/kg bw.(4) A study according to OECD Guideline 403 "Acute Inhalation Toxicity" is available. The study was performed with N-Butylbenzenesulphonamide 99.8% grade. The LC50 to rats after 4 hours exposure is greater than 4.066 mg/l. The N-Butylbenzenesulphonamide concentration at saturation (in air): 0.06 µg/l at 20°C.(2)

Repeated Dose Toxicity

For N-Butylbenzenesulphonamide oral, dermal and inhalation are considered to be possible exposure routes. As the substance is an involatile fluid, the inhalation route is expected to be less relevant. Therefore an oral 28-day toxicity study according to OECD 407 was performed. (11)

The dose levels for the 28-day study were selected to be 0, 50, 150 and 1000 mg/kg/day.

All high dose animals died prior to their scheduled necropsy. Up to 150 mg/kg/day the animals survived up to there scheduled termination.

High dose animals showed lethargy, hunched posture, uncoordinated movements, abnormal gait, salivation, emaciation, laboured respiration, swelling of the abdomen or head, and/or piloerection prior to sacrifice/death. All males

and most females of the high dose lost weight (up to 30%) or showed reduced weight gain and showed reduced food intake.

Degenerating nerve fibers were observed at low incidence and severity in the spinal cord and sciatic nerves at 150 and 1000 mg/kg/day. At 150 mg/kg/day, post mortem findings were confined to liver enlargement and hepatocyte hypertrophy, thymic atrophy and lymphocytolysis.

At 50 and 150 mg/kg/day, there were no changes at performance of functional observations, body weight and food consumption measurements, or alterations during clinical biochemistry investigations that were considered to be an effect of treatment. Also, at 50 mg/kg/day there were no treatment related macro- or microscopic findings.

The No Observed Adverse Effect Level (NOAEL) was established at 50 mg/kg/day.

Recommendation

No additional repeated dose studies are recommended.

Genetic Toxicity

Genetic Toxicology in vitro

An Ames metabolic activation test is available that assesses the potential mutagenic effect of the substance N-Butylbenzenesulphonamide.

It is concluded that no evidence of mutagenic potential was obtained in this bacterial (*Salmonella typhimurium*) test system in the presence or absence of metabolic activation. (7)

Genetic Toxicology in vivo

No data are available

Recommendation

It is recommended to perform a Chromosome aberration test (OECD Guideline 473)

Reproductive Toxicity

No studies are available

Developmental Toxicity

No studies are available

Recommendation

No data are available on reproductive or developmental toxicity. Therefore it is recommended to perform a Reproduction / Developmental Toxicity Screening Test, according to OECD 421.

Conclusion

With regard to the parameters demanded in the EPA HPV Challenge program, the available data fill the requirements for physicochemical, environmental fate and ecotoxicological parameters. Additional studies in these areas would not add significantly to our understanding of this material. For mammalian toxicity 2 tests are recommended, OECD 473 (Chromosome Aberration test) and OECD 421 (Reproduction / Developmental Screening test).

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